

a.) Amendment to the Specification

Please amend the paragraph at page 43, lines 5-18 to read as follows:

Compound (Ic-i) of Compound (Ic) where R^{3a} and R^{5a} are allyl may give Compound (Id) by treating Compound (Ic-i) with a nucleophilic reagent, for example, a combination of a palladium complex such as bis(triphenylphosphine)palladium(II) dichloride, etc. ~~and~~ with a formate such as ammonium formate, etc., with a typical metal hydride such as tributyltin hydride, etc., with a secondary amine such as morpholine, etc., and with an active methylene compound such as dimedone, etc., in an inert solvent. Examples of the inert solvent include tetrahydrofuran, acetic acid and 1,4-dioxane. These reactions are generally carried out at a temperature between room temperature and the boiling point of the solvent used for 1 minute to 24 hours.

Please amend the paragraph starting at page 83, line 25 and ending at page 84, line 16 to read as follows:

Human multiple myeloma-derived KMS-11 cells [In Vitro Cell. Dev. Biol., 25, 723 (1989)], which had been diluted with a 10 % fetal calf serum-containing RPMI 1640 (incubation medium) to 100,000 cell/mL, were put in a 6-well plastic plate for cell incubation (Nunc), in an amount of 3 mL/well. It is reported that the KMS-11 cells express a large quantity of FGFR3 (fibroblast growth ~~gene~~ factor receptor 3) as a result of translocation between the immunoglobulin gene in 14q32 and the FGFR3 gene in 4p16.3 [Blood, 90, 4062 (1997)]. A DMSO solution of a test compound that had been controlled to 10 mmol/L was further diluted with the incubation medium to 1/10 and 1/100, and added to the plate to a final concentration of 10 μ mol/L and 1.0 μ mol/L. In the control, the

test compound solution was not added. This was incubated in a 5 % carbon dioxide incubator at 37°C for 24 hours, and the cells were collected through centrifugation at 1000G for 5 minutes.

Please amend the paragraph at page 131, lines 7-21 to read as follows:

[2-Bromo-3,5-bis(methoxymethoxy)-6-phenylphenyl]methanol (553 mg, 1.44 mmol) obtained in the step 2 in Example 15 was dissolved in dichloromethane (20 mL), and triphenylphosphine (1.01 g, 3.85 mmol) and carbon tetrabromide (2.01 g, 6.06 mmol) were added thereto and stirred at room temperature for 2 hours. Water and aqueous saturated sodium hydrogencarbonate solution were added to the reaction mixture, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through silica gel column chromatography (n-hexane/ethyl acetate = 10/1 to 5/1 to 3/1) to obtain ~~3,4-dibromo-1,5~~ 4-Bromo-3-bromomethyl-1,5-bis(methoxymethoxy)-2-phenylbenzene (563 mg, 88 %).

Please amend the paragraph starting at page 177, line 21 and ending at page 178, line 8 to read as follows.

In an argon atmosphere, methyl 2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenylacetate (9.7 g, 26 mmol) obtained in the step 2 in Example 52 was dissolved in tetrahydrofuran (50 mL), and the solution was cooled to 4°C, and then tetrahydrofuran (50 mL) suspension of lithium aluminium hydride (0.13 g, 34 mmol) was dropwise added thereto, taking 10 minutes. The reaction mixture was stirred at 4°C for 1 hour, and then anhydrous sodium sulfate ~~10-hydrate~~ (20 g) was added thereto and stirred for 3 hours with heating up to room temperature. The white suspension was filtered, and the filtrate was concentrated under reduced pressure to obtain 2-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]ethanol (8.4 g, 94 %).

Please amend the paragraph at page 202, lines 2-10 to read as follows:

In the same manner as in the step 2 in Example 25, 4-bromo-1,5-bis(methoxymethoxy)-4-bromo-3-(3-methoxypropyl)-2-phenylbenzene ~~bis(methoxymethoxy)-4-bromo-3-(3-methoxypropyl)-2-phenylbenzene~~ bis(methoxymethoxy)-3-(3-methoxypropyl)-2-phenylbenzene (37.2 mg, 0.0875 mmol) was dissolved in ethanol (4 mL), and concentrated hydrochloric acid (0.1 mL) was added thereto and stirred at 60°C for 1.1 hours. The reaction liquid was concentrated under reduced pressure, and the resulting residue was purified through partitioning thin-layer chromatography (chloroform/methanol = 20/1) to obtain Compound 97 (28.7 mg, 97 %).

Please amend the paragraph at page 259, lines 16-23 to read as follows:

In the same manner as in the step 1 in Example 64, 1-[2-(2-methoxyethoxy)ethyl]-3,5-bis(methoxymethoxy)benzene (6.6 g, 55 %) was obtained from 2-[3,5-bis(methoxymethoxy)phenyl]ethanol (5.4 g, 22 mmol) obtained in the step 1 in Example 116, using 60 % sodium hydride/mineral oil dispersion (1.8 g, 45 mmol), 2-bromomethoxyethyl 2-bromomethoxyethane (6.2 mL, 34 mmol) and N,N-dimethylformamide (70 mL).

Please amend the paragraph at page 264, lines 9-22 to read as follows:

1-[(2-(2-Methoxyethoxy)ethyl)]-3,5-bis(methoxymethoxy)-2-phenylbenzene (410 mg, 1.2 mmol) obtained in the step 1 in Example 136 was dissolved in dichloromethane (10 mL), and pyridine (0.10 mL, 1.2 mmol) and trifluoromethanesulfonic acid anhydride (0.20 mL, 1.2 mmol) were added thereto with cooling with ice, and stirred at the same temperature for 1 hour. The reaction liquid was neutralized with diluted hydrochloric acid, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, dried over sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin layer silica gel column chromatography (n-hexane/ethyl acetate = 2/1) to obtain Compound 140 (150 mg, yield 30 %).

Please amend the paragraph at page 283, lines 11-22 to read as follows:

3,5-Bis(methoxymethoxy)-1-[(2-(2-methoxyethoxy)ethyl)]-2-phenylbenzene (0.080 g, 0.28 mmol) obtained in the step 1 in Example 136 was dissolved in N,N-dimethylformamide (2.0 mL), and sulfamoyl chloride (64 g, 0.56 mmol) was added thereto and stirred at room temperature for 1 day. The reaction liquid was poured into water, and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer silica gel column chromatography (chloroform/methanol = 15/1) to obtain Compound 152 (3.6 mg, 3.5 %).

Please amend the paragraph at page 284, lines 15-22 to read as follows:

In the same manner as in the step 1 in Example 64, 2-ethyl-1-[2-(2-methoxyethoxy)ethyl]-3,5-bis(methoxymethoxy)benzene (510 mg, 45 %) was obtained from 2-[2-ethyl-3,5-bis(methoxymethoxy)phenyl]ethanol (1.0 g, 3.7 mmol) obtained in the above, using 60 % sodium hydride/mineral oil dispersion (310 mg, 7.8 mmol), 2-bromomethoxyethyl 2-bromomethoxyethane (1.1 mL, 12 mmol) and N,N-dimethylformamide (70 mL).

Please amend the paragraph at page 354, lines 12-24 to read as follows.

4-Ethyl-1,5-bis(methoxymethoxy)-2-phenyl-3-[2-(pyridin-3-ylmethoxy)ethyl]benzene (78 mg, 0.18 mmol) obtained in the above was dissolved in methanol (10 mL), and hydrochloric acid (1 mL, 6 mol/L) was added thereto and stirred

for a half day at room temperature. The reaction liquid was neutralized with aqueous 1 mol/L sodium hydroxide solution, and then extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (developed with n-hexane/ethyl acetate = 1/1) to obtain Compound 188 (28 mg, 41 %).

Please amend the paragraphs starting at page 365, line 3 and ending at page 366, line 4 to read as follows:

In an argon atmosphere, 2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenylacetic acid (86 mg, 0.27 mmol) obtained in the above was dissolved in dichloromethane (10 mL), and diethanolamine (75 mg, 0.70 mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (63 mg, 0.33 mmol) and 1-hydroxybenzotriazole hydrate (50 mg, 0.33 mmol) were added thereto and stirred at room temperature for 3 hours. The reaction liquid was concentrated under reduced pressure, and purified through preparative thin-layer column chromatography (chloroform/methanol = 15/1) to obtain 2-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]-N,N-bis(2-hydroxyethyl)acetamide (56 mg, 51 %).

APCI-MS (m/z): 448 (M+H)⁺.

(Step 3)

2-[2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]-N,N-bis(2-hydroxyethyl)acetamide (78 mg, 0.18 mmol) obtained in the above was dissolved in

methanol (3 mL), and 4 mol/L hydrogen chloride (1 ml) was added thereto and stirred at room temperature for 2 hours. The reaction liquid was neutralized with aqueous 1.0 mol/L sodium hydroxide solution, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (n-hexane/ethyl acetate = 1/1) to obtain Compound 198 (22 mg, 13 %).

Please amend the paragraph starting at page 366, line 14 and ending at page 367, line 2 to read as follows:

Methyl 2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenylacetate (19 mg, 0.050 mmol) obtained in the step 2 in Example 52 was dissolved in tetrahydrofuran (10 mL), and allylmagnesium bromide (0.20 mL, 1.0 mol/L) was added thereto and stirred at room temperature for 1 hour. The reaction liquid was neutralized with hydrochloric acid (1.0 mol/L), and then extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (n-hexane/ethyl acetate = 4/1) to obtain 4-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]hept-1,6-dien-4-ol (32 mg, quantitative).

Please amend the paragraph starting at page 367, line 9 and ending at page 368, line 1 to read as follows:

In an argon atmosphere, 4-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]hept-1,6-dien-4-ol (32 mg, 0.75 mmol) obtained in the above was dissolved in tetrahydrofuran (10 mL), and borane-tetrahydrofuran complex (0.20 mL, 1.0 mol/L) was added thereto at -78°C, then gently heated up to room temperature, and stirred for 6 hours. Aqueous saturated sodium bicarbonate solution (1.2 mL) and aqueous hydrogen peroxide (1.2 mL) were added to the reaction mixture, and stirred at the same temperature for 1 hour. Water was added to the reaction liquid, and extracted with ethyl acetate. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (n-hexane/ethyl acetate = 1/1) to obtain 4-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]heptane-1,4,7-triol (13 mg, 37 %).

Please amend the paragraph at page 368, lines 9-22 to read as follows:

4-[2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]heptane-1,4,7-triol (50 mg, 0.11 mmol) obtained in the above was dissolved in methanol (5.0 mL), and 1,4-dioxane solution (1.0 mL) of 4 mol/L hydrogen chloride was added thereto and stirred at room temperature for 2 hours. The reaction liquid was neutralized with aqueous 1 mol/L sodium hydroxide solution, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting

residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 199 (21 mg, 55 %).

Please amend the paragraph at page 369, lines 6-24 to read as follows:

2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenylacetic acid (70 mg, 0.2 mmol) obtained in the step 1 in Example 198 was dissolved in N,N-dimethylacetamide (10 mL), and potassium carbonate (55 mg, 0.4 mmol) and methyl isocyanoacetate (79 mL, 0.4 mmol) were added thereto and stirred at room temperature for 5 minutes.

Diphenylphosphorylamide (0.040 mL, 0.22 mmol) was added to the reaction mixture, and stirred at 0°C for 2 hours. With heating up to room temperature, the reaction mixture was further stirred for 12 hours, and then neutralized with 1.0 mol/L hydrochloric acid, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (n-hexane/ethyl acetate = 1/1) to obtain methyl 5-{{2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl}methyl}-1,3-oxazole-4-carboxylate (38 mg, 48 %).

Please amend the paragraph at page 370, lines 2-15 to read as follows:

Methyl 5-{{2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl}methyl}-1,3-oxazole-4-carboxylate (43 mg, 0.10 mmol) obtained in the above was dissolved in methanol (5.0 mL), and 1,4-dioxane solution (1.0 mL) of 4.0 mol/L hydrochloric acid was

added thereto and stirred at 40°C for 2 hours. The reaction liquid was neutralized with aqueous 1.0 mol/L sodium hydroxide solution, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified preparative through thin-layer column chromatography (n-hexane/ethyl acetate = 1/1) to obtain Compound 200 (11 mg, 31 %).

Please amend the paragraph starting at page 370, line 24 and ending at page 371, line 12 to read as follows:

In an argon atmosphere, 2-[3,5-bis(benzyloxy)-2-ethyl-6-phenylphenyl]ethanol (44 mg, 0.10 mmol) obtained in the step 4 in Example 179 was dissolved in dichloromethane (3.0 mL), and tri-O-benzyl-D-glucal (0.62 mL, 0.15 mol/L) and triphenylphosphonium bromide (10 mg, 0.03 mmol) were added thereto and stirred at room temperature for 12 hours. Water was added to the reaction liquid, and extracted with a mixed solvent of chloroform and methanol (9/1). The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (n-hexane/ethyl acetate = 1/1) to obtain a glycoside (42 mg, 49 %).

Please amend the paragraph at page 371, lines 15-23 to read as follows:

The glycoside (42 mg, 0.049 mmol) obtained in the above was dissolved in ethyl acetate (20 mL), and in a hydrogen atmosphere, 10 % palladium-carbon (42 mg) was added thereto and stirred at room temperature for 3 days. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 201 (21 mg, 100 %).

Please amend the paragraph starting at page 378, line 25 and ending at page 379, line 13 as follows:

(5-{{2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl}methyl}-1,3-oxazol-4-yl)methanol (52 mg) obtained in the above was dissolved in methanol (4.0 mL), and 1,4-dioxane solution (1.0 mL) of 4.0 mol/L hydrochloric acid was added thereto and stirred at room temperature for 3 hours. The reaction liquid was neutralized with aqueous 1 mol/L sodium hydroxide solution, and then extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 208 (14 mg, 29 %).

Please amend the paragraph starting at page 380, line 20 and ending at page 381, line 8 to read as follows:

Methyl 5-{2-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]ethyl}-1,3-oxazole-4-carboxylate (89 mg, 0.20 mmol) obtained in the above was dissolved in methanol (5.0 mL), and 1,4-dioxane solution (1.0 mL) of 4.0 mol/L hydrochloric acid was added thereto and stirred at 40°C for 4 hours. The reaction liquid was neutralized with aqueous 1 mol/L sodium hydroxide solution, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (n-hexane/ethyl acetate = 1/1) to obtain Compound 209 (50 mg, 69 %).

Please amend the paragraph at page 382, lines 11-23 to read as follows:

(5-{2-[2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]ethyl}-1,3-oxazol-4-yl)methanol (200 mg) was dissolved in methanol (5.0 mL), and 1,4-dioxane solution (1 ml) of 4.0 mol/L hydrochloric acid was added thereto and stirred at room temperature for 3 hours. The reaction liquid was neutralized with aqueous sodium hydroxide solution (1 mol/L), and then extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 210 (53 mg, 39 %).

Please amend the paragraph at page 383, lines 7-19 to read as follows:

~~2-[2-Ethyl-3,5-bis(benzyloxy)-6-~~ 2-[3,5-Bis(benzyloxy)-2-ethyl-6-
phenylphenyl]ethanal (120 mg, 0.28 mol) obtained in the step 1 in Example 218 was dissolved in dichloromethane (10 mL), and glycerin (0.15 mL, 1.0 mol) and p-toluenesulfonic acid (15 mg, 0.1 mol) were added thereto and stirred at room temperature for 4 hours. The reaction liquid was neutralized with aqueous saturated sodium bicarbonate solution, and then extracted with ethyl acetate. The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure to obtain (2-{[3,5-bis(benzyloxy)-2-ethyl-6-phenylphenyl]methyl}-1,3-dioxolan-4-yl)methanol (150 mg, 100 %).

Please amend the paragraph starting at page 384, line 13 and ending at page 385, line 3 to read as follows:

In an argon atmosphere, methyl 3-[2-iodo-3,5-bis(methoxymethoxy)-6-phenylphenyl]propanoate (2.9 g, 6.0 mmol) obtained in the step 1 in Example 186 was dissolved in toluene (100 mL), and bis(tri-o-tolylphosphine)palladium(II) dichloride (940 mg, 1.2 mmol) and tributylvinyltin (3.8 g, 12 mmol) were added thereto and stirred at 100°C for 12 hours. The reaction liquid was poured into aqueous ammonium fluoride solution, and stirred for one full day, and then filtered through Celite. Activated charcoal was added to the filtrate and stirred for 3 hours, and then filtered through Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was purified through preparative silica gel column chromatography (n-hexane/ethyl acetate = 8/1) to

obtain methyl 3-[3,5-bis(methoxymethoxy)-6-phenyl-2-vinylphenyl]propanoate (2.0 g, 87 %).

Please amend the paragraph starting at page 386, line 16 and ending at page 387, line 6 to read as follows:

3-[2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]propanoic acid (250 mg, 0.67 mmol) obtained in the above was dissolved in dichloromethane (10 mL), and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (130 mg, 0.67 mmol) and 1-hydroxybenzotriazole hydrate (100 mg, 0.67 mmol) were added thereto and stirred at room temperature for 1 hour. Methanol solution (3.0 mL) of 7.0 mol/L ammonia was added to the reaction solution, and stirred at room temperature for 3 hours. Water was added to the reaction liquid, and extracted with chloroform. The organic layer was dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative silica gel column chromatography (ethyl acetate/n-hexane = 2/1) to obtain 3-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]propanamide (190 mg, 76 %).

Please amend the paragraph starting at page 388, line 11 and ending at page 389, line 3 to read as follows:

2-[2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]ethanal (88 mg, 0.26 mmol) obtained in the step 1 in Example 177 was dissolved in toluene (10 mL), and dimethyl malonate (0.059 mL, 0.52 mmol), piperidine (0.051 mL, 0.52 mmol) and acetic acid (0.060 mL, 1.0 mmol) were added thereto in order, and stirred at room temperature for

19 hours. Water was put into the reaction liquid, and extracted with ethyl acetate. The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer silica gel column chromatography (n-hexane/ethyl acetate = 2/1) to obtain a mixture of methyl 4-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]-2-(methoxycarbonyl)but-2-enoate and dimethyl 2-{2-[2-ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]vinyl}di-propanoate (about 1/1).

Please amend the paragraph starting at page 389, line 20 and ending at page 390, line 9 to read as follows:

The mixture (20 mg, 0.054 mol) obtained in the above was added to diethyl ether suspension (50 mL) of lithium aluminium hydride (20 mg, 0.54 mol), and with cooling with ice, this was stirred for 1 hour, and then lithium aluminium hydride (24 mg, 0.64 mol) was added thereto and stirred at room temperature for 2 hours. 1.0 mol/L hydrochloric acid (4.0 mL) was added to the reaction mixture, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 213 (5.2 mg, 26 %) and Compound 214 (2.0 mg, 12 %).

Please amend the paragraph at page 391, lines 1-14 to read as follows:

Tetrahydrofuran solution (10 mL) of Compound 213 (82 mg) obtained in Example 213 was added to tetrahydrofuran suspension (10 mL) of lithium aluminium hydride (8.1 mg, 0.32 mmol) and stirred for 1 hour with cooling with ice, and then lithium aluminium hydride (65 mg, 2.5 mol) was added thereto and stirred at room temperature for 2 hours. 1.0 mol/L hydrochloric acid (4.0 mL) was added to the reaction mixture, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 215 (4.0 mg, 5.7 %).

Please amend the paragraphs starting at page 394, line 2 and ending at page 395, line 1 to read as follows:

In an argon atmosphere, 2-[3,5-bis(benzyloxy)-2-ethyl-6-phenylphenyl]ethanol (88 mg, 0.20 mmol) obtained in the step 4 in Example 179 was dissolved in dichloromethane (3.0 mL), and tri-O-benzyl-D-galactal (0.92 mg, 0.15 mol/L) and triphenylphosphonium bromide (20 mg, 0.060 mmol) were added thereto and stirred at room temperature for 40 hours. Water was added to the reaction liquid, and extracted with a mixed solvent of chloroform and methanol (9/1). The organic layer was washed with aqueous saturated sodium chloride solution, and dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. The resulting residue was

purified through preparative thin-layer column chromatography (n-hexane/ethyl acetate = 1/1) to obtain a glycoside (100 mg, 58 %).

FAB-MS (m/z): 854 (M⁺)⁺.

(Step 2)

The glycoside (100 mg, 0.12 mmol) obtained in the above was dissolved in ethyl acetate (10 mL), and in a hydrogen atmosphere, 10 % palladium-carbon (100 mg) was added thereto and stirred at room temperature for 3 days. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 216 (36 mg, 81 %).

Please amend the paragraph at page 397, lines 13-25 to read as follows:

2-{3-[2-Ethyl-3,5-bis(methoxymethoxy)-6-phenylphenyl]propyl}propane-1,3-diol (50 mg, 0.11 mmol) obtained in the above was dissolved in methanol (5.0 mL), and 1,4-dioxane solution (1.0 mL) of 4.0 mol/L hydrochloric acid was added thereto and stirred at room temperature for 2 hours. The reaction liquid was neutralized with aqueous 1 mol/L sodium hydroxide solution, and extracted with chloroform. The organic layer was washed with aqueous saturated sodium chloride solution, and the solvent was evaporated away under reduced pressure. The resulting residue was purified through preparative thin-layer column chromatography (chloroform/methanol = 9/1) to obtain Compound 217 (44 mg, 42 %).

Please amend the paragraph starting at page 402, line 19 and ending at page 403, line 3 to read as follows:

~~1,5-Bis(benzyloxy)-4-ethyl-3-[2-(oxiran-2-ylmethyl)ethyl]-2-phenylbenzene~~ 1,5-Bis(benzyloxy)-4-ethyl-3-[2-(oxiran-2-ylmethoxy)ethyl]-2-phenylbenzene (230 mg, 0.45 mmol) obtained in the above was dissolved in ethyl acetate (10-mL), and 10 % palladium-carbon (50 % wet., 200 mg) was added thereto and stirred in a hydrogen atmosphere at room temperature for 6 hours. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was purified through silica gel column chromatography (ethyl acetate/n-hexane = 1/2 to 1/1) to obtain Compound 219 (83 mg, 56 %).

Please amend the paragraph starting at page 471, line 24 and ending at page 472, line 9 to read as follows:

In the same manner as in Example 245, methyl 2-[5-(N,N-diethylaminomethyl)furan-2-yl]-3,5-bis(methoxymethoxy)phenylacetate was obtained from methyl 2-(5-formylfuran-2-yl)-3,5-bis(methoxymethoxy)phenylacetate (58 mg, 0.16 mmol) obtained in the step 4 in Example 245, using diethylamine (0.03 mL, 0.41 mmol), sodium triacetoxyborohydride (150 mg, 0.71 mmol) and 1,2-dichloroethane (3.0 mL). The resulting compound was processed with methanol (1.0 mL) and 1,4-dioxane solution (1.0 mL) of 4 mol/L hydrogen chloride to obtain ~~Compound 251~~ Compound 252 (21 mg, 39 %).

Please amend the paragraph starting at page 483, line 19 and ending at page 484, line 3 to read as follows:

Methyl 2-[5-(hydroxymethyl)furan-2-yl]-3,5-bis(methoxymethoxy)phenylacetate (70 mg, 0.19 mmol) obtained in the above was dissolved in 2-propanol (3.0 mL), and 1,4-dioxane solution (3.0 mL) of 4 mol/L hydrogen chloride was added thereto and stirred at room temperature for 20 minutes. The reaction liquid was concentrated under reduced pressure, and the resulting residue was purified through partitioning thin-layer chromatography (methanol/chloroform = 1/9) to obtain Example Compound 258 (52 mg, 98 %).

Please amend the paragraph at page 503, lines 12-17 to read as follows:

In the same manner as in the step 4 in Example 1, Compound 268 (60 mg, 82 %) was obtained from methyl 2-[5-(3-hydroxybutyl)furan-2-yl]-3,5-bis(methoxymethoxy)phenylacetate 2-[5-(3-hydroxyiminobutyl)furan-2-yl]-3,5-bis(methoxymethoxy)phenylacetate (96 mg, 0.22 mmol) obtained in the above, using methanol (1.0 mL) and 1,4-dioxane solution (1.0 mL) of 4 mol/L hydrogen chloride.

Please amend the paragraph at starting at page 511, line 23 and ending at page 512, line 19 to read as follows:

5-Bromo-1-ethyl-2,4-bis(methoxymethoxy)benzene (570 mg, 1.9 mmol) obtained in the above was dissolved in tetrahydrofuran (15 mL), and with stirring at -78°C, n-hexane solution of 1.5 mol/L n-butyllithium (1.9 mL, 2.9 ~~mL~~ mmol) was added thereto

and stirred for 30 minutes. 2-Fluoro-4-methoxybenzaldehyde (430 mg, 2.8 mmol) was added to the reaction liquid, and stirred for 1 hour. Aqueous saturated ammonium chloride solution was added to the reaction liquid, heated up to room temperature, and then extracted twice with ethyl acetate. The organic layer was washed with aqueous saturated sodium chloride solution, then dried over anhydrous sodium sulfate, and the solvent was evaporated away under reduced pressure. Dichloromethane (30 mL) and pyridinium dichromate (1.0 g, 2.7 mmol) were added to the resulting residue, and stirred at room temperature for 18 hours. The reaction mixture was diluted with ether, and filtered through Celite. The filtrate was concentrated under reduced pressure, and the resulting residue was purified through silica gel column chromatography (ethyl acetate/n-hexane = 1/4 to 1/2) to obtain 5-ethyl-2,4-bis(methoxymethoxy)phenyl 2-fluoro-4-methoxyphenyl ketone (450 mg, 65 %).

Please amend line 3 at page 544 to read as follows:

~~(Step 3)~~ (Step 2)

Please amend the paragraph at page 546, lines 6-8 to read as follows:

5- {[(4R,5R)-4,5-bis(hydroxymethyl)-1,3-dioxolan-2-yl]methyl }-4-(3-carbamoylphenyl)-6-ethylbenzene-1,3-diol ~~(Compound 294)~~ (Compound 295)

Please amend the paragraph at page 551, lines 17-19 to read as follows:

5- {[(4S,5S)-4,5-bis(hydroxymethyl)-1,3-dioxolan-2-yl]methyl} -4-(3,4-difluorophenyl)-6-ethylbenzene-1,3-diol (~~Compound 297~~) (Compound 299)

Please amend the paragraph at page 592, lines 5-10 to read as follows:

In the same manner as in the step 4 in Example 309, Compound 321 (110 mg, 66 %) was obtained from ~~4,5-bis(benzyloxy)-2-ethyl-1-[2-(3-hydroxypyrrolidin-1-yl)ethyl]-6-phenylbenzene~~ 3,5-bis(benzyloxy)-2-ethyl-1-[2-(3-hydroxypyrrolidin-1-yl)ethyl]-6-phenylbenzene (260 mg, 0.51 mmol) obtained in the above, using 10 % palladium-carbon (50 % wet., 20 mg) and tetrahydrofuran (10 mL).

Please amend the paragraph at page 603, lines 4-5 to read as follows:

Methyl 2-ethyl-3,5-dihydroxy-6-(5-phenyl-1,3-oxazol-2-yl)phenylacetate (~~Compound 330~~) (Compound 329)

Please amend the paragraph at page 609, lines 20-25 to read as follows:

In the same manner as in the step 4 in Example 1, ~~Compound 330~~ Compound 329 (3 mg, 71 %) was obtained from methyl 2-ethyl-3,5-bis(methoxymethoxy)-6-(5-phenyloxazol-2-yl)phenylacetate (7 mg, 0.016 mmol) obtained in the above, using methanol (2.0 mL) and 1,4-dioxane solution (1.0 mL) of 4 mol/L hydrogen chloride.

Please amend the paragraph at page 612, lines 17-23 to read as follows:

In the same manner as in the step 4 in Example 1, ~~Compound 329~~

Compound 330 (28 mg, 63 %) was obtained from 3-{2-[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]ethyl}-4-ethyl-2-(6-methoxy-1H-indazol-3-yl)-1,5-

bis(methoxymethoxy)benzene (60 mg, 0.11 mmol) obtained in the above, using methanol (2.0 mL) and 1,4-dioxane solution (1.0 mL) of 4 mol/L hydrogen chloride.